GC Biopharma

Global Leader in the Biopharma Industry

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CMO

We are GC Biopharma

GC Biopharma Major Business Portfolio

GC Biopharma has been accumulating expertise in plasma derivatives, vaccines, recombinant proteins, and chemical prescription drugs.

Innovative rare disease medicines	Hunter syndrome treatment
Globally leading plasma-derived medicines	Albumin, Human immunoglobulin
Globally leading diverse vaccines	Varicella and Flu vaccines
Trusted expertise in aseptic filling solution	CMO (fill & finish)
Total solution for mRNA medicines	CDMO (mRNA/LNP)

GC Biopharma At a Glance

It is our MISSION to contribute to the healthy lives of humankind and it is our VISION to be a global leader in the health industry.

1967 Established

1989 IPO (S. Korea)

6,256+	Empolyees
$16.96 Bil	'24 Revenue*
150+	Commercial Products
68	Export Countries

*Consolidated Accounting Standards

No.1
- Plasma derivatives
- Vaccines
- Rare disease business in S. Korea

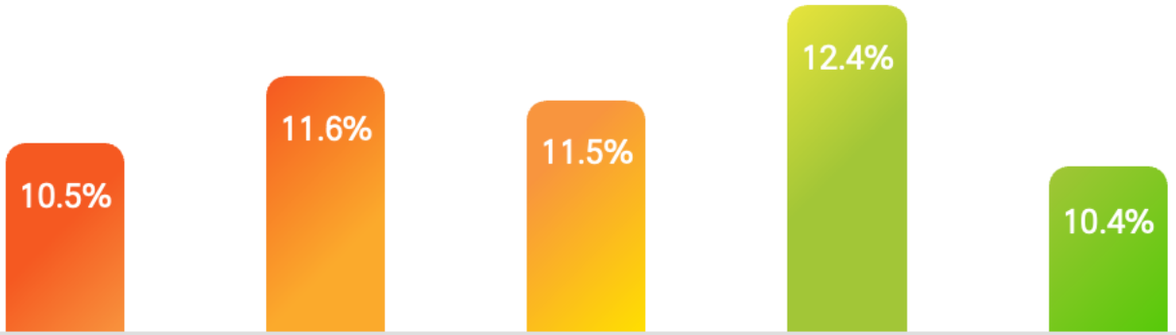
2023
- IVIG 10% FDA Approval
- MPS IIIA Orphan Drug Designation

2030
- Global sales + 1.9 Bil USD
- Over +68 Countries

Research & Development Investments

GC Biopharma's researchers Continue to rise To the challenge of saving lives

R&D to Revenue Ratio



Category	Unit	2020	2021	2022	2023	2024
R&D Costs	USD million	109.5	122.1	114.4	120.1	96.6

R&D workforce
[As of June 2024]

Total **428** persons

- **Master's / Doctorate** : 299 persons
- **Bachelor's** : 82 persons
- **Others** : 47 persons

Global Network

Mission to the healthy lives & Vision to be a global leader

8 Global operations + 3 branch offices across the world

Medicines Access

Unlimited dedication to the development of safer and more effective treatments

Core Products

Vaccines

- Flu Vaccine
- Varicella Vaccine
- Td Vaccine & 5 Others

Blood Plasma Derived

- Albumin
- Human Immunoglobulin G
- Human Hepatitis B
- Immunoglobulin (HBIG) + 10 Others

Rare Disease

- ERT for Hunter syndrome
- Hemophilia A/B type
- Alagille syndrome

Tumor	Treatment for Severe Neutrophil Reduction
Metabolic & Cardiovascular	High blood pressure, Dyslipidemia, Diabetes
OTC Drugs	Vitamins, Painkillers, Patches

R&D Pipeline (as of October 2025)

GC Biopharma

Business key update

	Preclinical	Phase I	Phase II	Phase III	Registration / Approved
Plasma Derivatives	GC5125 vWF deficiency GC5136 PID (SC IVIG)			GC5107 US PID- IVIG (Pediatric)	GC5107 US PID - IVIG
Vaccines	GC4002 mRNA Flu vaccine GC3114B TIV-HD	GC4006A mRNA COVID vaccine	MG1120/CRV-101 US Shingles vaccine MG1111 Varicella vaccine (2 dose) GC3111 Tdap vaccine		MG1111 Varicella vaccine GC1109 Anthrax vaccine GC1109 H5N1 pandemic vaccine
Innovative medicines	GC4003 (mRNA) SSADH deficiency GC1126 TTP GC2126 Gangliosidosis	MG1113 Hemophilia A/B GC1123 KR Hunter syndrome (severe type) GC1130 US MPSIIIA (Ph1)	GC1134 US Fabry disease (Ph1/2)	GC1138 Glanzmann's disease	GC2127 Alagille syndrome GC1101 China Hemophilia A GC1111 Hunter syndrome

#VARICELLA
#VACCINE
#BARYCELA inj.

#MAV/06 #World 1st Antibiotic-free varicella vaccine #Prevent household infections

BARYCELA inj.

GC Biopharma

Prepare with BARYCELA inj. for effective varicella prevention.

- Upgraded varicella vaccine through accumulated technology
- The world's first antibiotic-free varicell vaccine
- Vaccine Stability
- Improved safety risk through the aseptic processing and single-use systems

History

GC Biopharma, the leader of Korea's vaccine development

1983 — **HepavaxB** World's third vaccine for hepatitis B (Korea's first)

1988 — **Hantavax** World's first vaccine for hemorrhagic fever with renal syndrome

1993 — **Suduvax** World's second varicella vaccine

2009 — **Completed construction of Hwasun plant,** Korea's first manufacturing facility dedicated to vaccine production

2015 — **GCFLU Quadrivalent** Korea's first quadrivalent influenza vaccine (World's fourth)

2016 — **GCC Td Vaccine** Korea's first Td vaccine

2021 — **BARYCELA inj.** World's first antibiotic-free varicella vaccine

2023 — **WHO PQ** was approved in 2023 Feb.

BARYCELA inj.

GC Biopharma

Over the past 30 years, more than 30 million doses of GC Biopharma's varicella vaccine

have been used worldwide and based on our accumulated R&D know-how, an upgraded varicella vaccine, BARYCELA inj. has recently been developed.

30 years

30 million

Over the past 30 years, 30 million doses of Varicella Vaccine-GCC inj. were used in more than 30 countries including Republic of Korea, Brazil, Turkey, Argentina, Saudi Arabia, Vietnam and so on.

BARYCELA inj. has not only increased virus content, but also significantly improved stability.

Brand name	**SUDUVAX inj. (Varicella vaccine-GCC inj.)** (First approval date: 05 June 1993)
Virus Strain	**MAV/06** (isolated from a Korean patient and attenuated)
Virus content	**≥1,400 PFU**
Manufacturing Process	• **Manual process** • **Multi-use system** (Open process, Class 100) • **Antibiotics contained**

UPGRADE

BARYCELA inj. (First approval date: 02 March 2020)
MAV/06 (isolated from a Korean patient and attenuated)
≥3,800 PFU
• **Automated process** (Purification, Fill & Finish) • **Single-use system** (Closed process, Class 100,000) • **Antibiotic free** • **Improved formulation for stability**

BARYCELA inj.

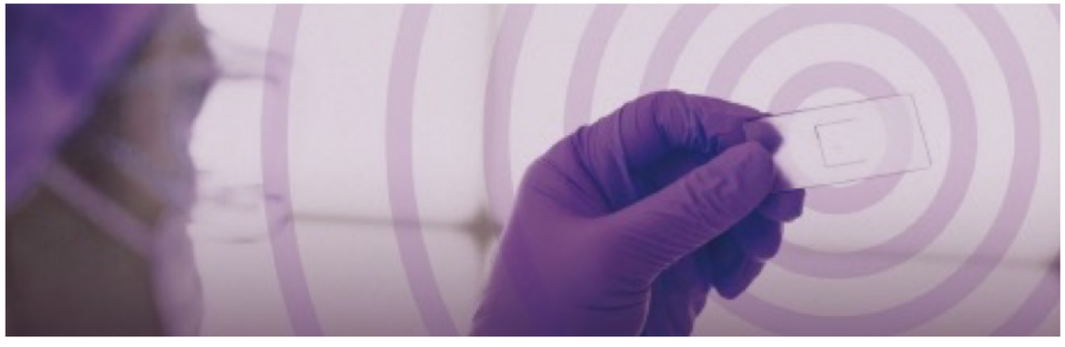
GC Biopharma

BARYCELA inj. was demonstrated to have a seroconversion rate non-inferior to that of the control vaccine in a multinational phase Ⅲ clinical trial.

Seroconversion rate (SCR) at 42 days after vaccination

	Conversion criteria		MG1111[1] N= 239	Control[2] N = 239	Difference	P-value
SCR (%)	**FAMA titer ≥1:4**		**97.91** (95.19, 99.32)[3]	**99.16** (97.01, 99.90)[3]	**-1.3** (-4.03, 1.22)[4]	0.2533
	Sub-analysis	Subjects aged 12 M to ≤23 M	**97.96** (94.86, 99.44)[3]	**100.00** (98.11, 100.00)[3]	**-2.0** (-5.13, 0.27)[4]	-
	Sub-analysis	Subjects aged 24 M to ≤12 Y	**97.67** (87.71, 99.94)[3]	**95.65** (85.16, 99.47)[3]	**2.0** (-8.21, 12.38)[4]	-
	FAMA titer ≥1:16		**95.65** (93.51, 98.54)[3]	**98.33** (95.77, 99.54)[3]	**-1.7** (-4.95, 1.36)[4]	-

1. Development name of BARYCELA inj. 2. Varivax 3. Two-sided 95% confidence interval (CI) is calculated using exact binomial method.
4. 95% confidence interval for rate difference is calculated using Newcombe-Wilson score method.



BARYCELA inj. showed a similar safety profile to that of the control vaccine.

Safety Assessments

	MG1111[1](N=258)		Control[2](N=257)		P-value
	N(%)	event	N(%)	event	
Total AEs	202(78.3)	1109	192(74.7)	1071	0.337
Solicited local AEs	122(47.3)	462	132(51.4)	535	0.355
Solicited systemic AEs	93(36.0)	450	83(32.3)	379	0.370
Treatment-related AEs	160(62.0)	838	162(63.0)	902	0.811
Treatment-related solicited AEs	153(59.3)	789	154(59.9)	864	0.886
Treatment-related unsolicited AEs	41(15.9)	49	27(10.5)	38	0.071
SAEs	29(11.2)	39	21(8.2)	33	0.240
Treatment-related SAEs	3(1.2)	5	4(1.6)	7	0.724

1. Development name of BARYCELA inj. 2. Varivax. AE, adverse event; SAE, serious adverse event

BARYCELA inj.

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BARYCELA inj. is the world's only
antibiotic-free varicella vaccine.

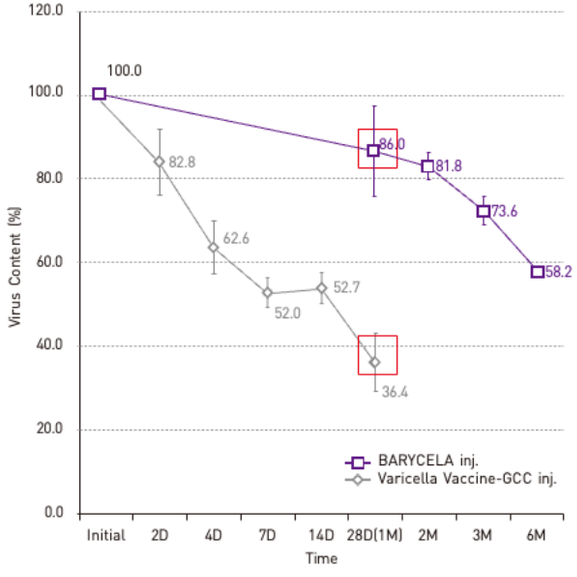
ANTIBIOTIC-FREE

Improved product stability by addition of urea

Accelerated stability test (25.0 ± 2.0°C/60.0 ± 5.0% RH*)
Varicella Vaccine-GCC inj. vs BARYCELA inj. (1 month) = 36.4% : 86.0%

Formula (product)	SUDUVAX inj. (Varicella vaccine-GCC inj.)	BARYCELA inj.
Sucrose	25 mg	**18.21 mg**
Glycine	2.5 mg	**1.82 mg**
Sodium L-glutamate hydrate	0.55 mg	**0.40 mg**
Gelatin	12.5 mg	**8.74 mg**
L-Cysteine	0.25 mg	**0.18 mg**
EDTA or its hydrate	0.25 mg	**0.18 mg**
$Na_2HPO_4 \cdot 12H_2O$(buffer)	Appropriate amount	**1.14 mg**
$NaH_2PO_4 \cdot 2H_2O$(buffer)	Appropriate amount	
Potassium phosphate monobasic(buffer)		**0.06 mg**
Urea		**0.87 mg**
Volume per dose (mL)	0.5 mL	**0.5 mL**

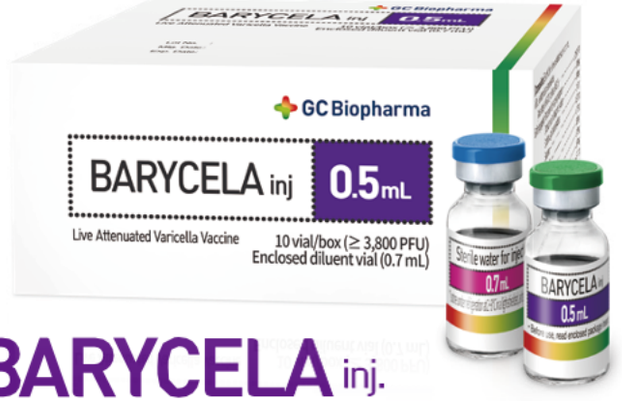
*RH, relative humidity



BARYCELA inj. has improved product safety risk
through the introduction of aseptic processing, automated systems, and single-use systems.

Bulk | Final Bulk | Filling | Lyophilization | Capping | Inspection | Packaging | Drug Product

Bulk | Final Bulk | Filling | Lyophilization | Capping



BARYCELA inj.

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HEALTHY LIFE AHEAD

GC FLU Quadrivalent Pre-filled Syringe inj.

GC Biopharma

GCFLU Quadrivalent

GCFLU Quadrivalent is an egg-based seasonal influenza vaccine developed and manufactured by GC Biopharma, which is a WHO PQ vaccine.[1]

Product Profile

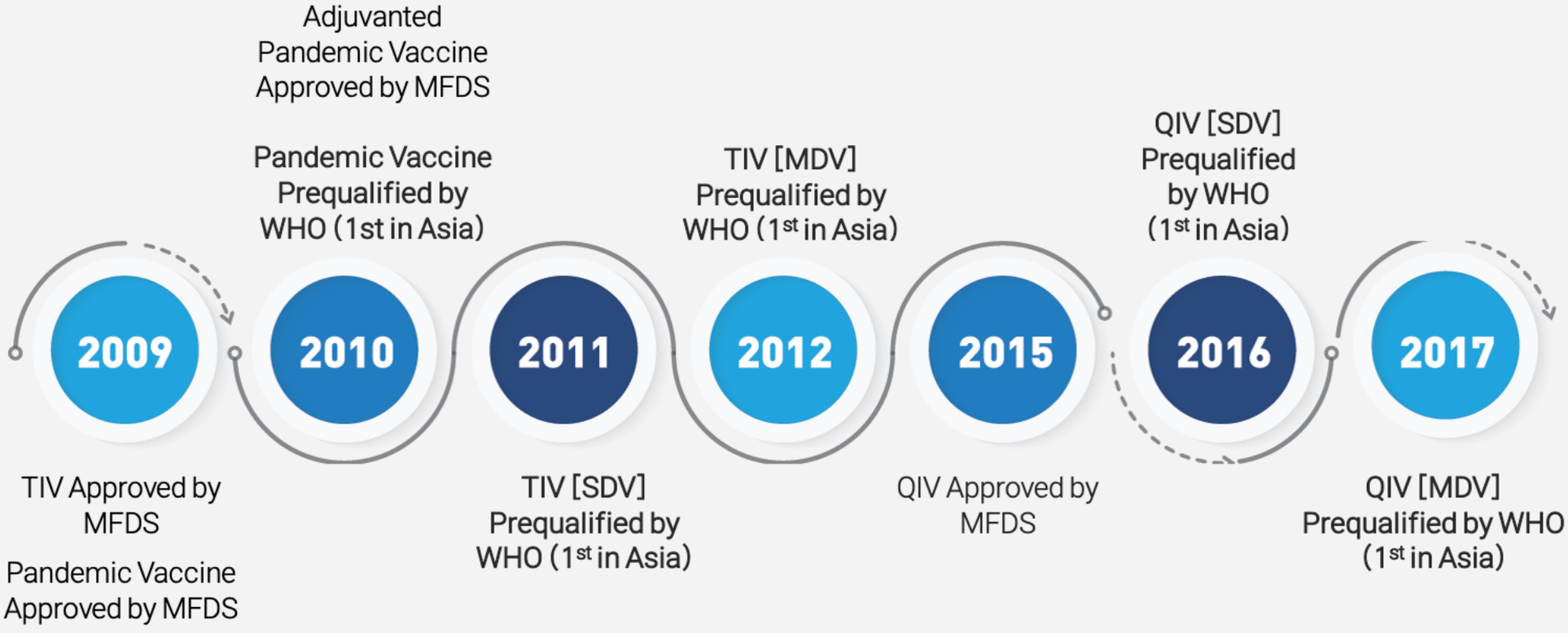
Type	Description
Vaccine Type	**Inactivated Quadrivalent Seasonal Influenza Vaccine**
Vaccine Strain	**WHO Recommended Strains**
Virus Culture	**Fertilized Egg**
Administration	**0.5mL Intramuscular Injection**
Age Indication	**Persons Aged 6 Months and Older**
Container	**Pre-filled Syringe**
Preservative	**Thimerosal Free**
Manufacturer	**GC Biopharma**

GC FLU Quadrivalent Pre-filled Syringe inj.

GC Biopharma

History

GCFLU TIV and GCFLU QIV have obtained the WHO prequalification. [2]



GC FLU Quadrivalent Pre-filled Syringe inj.

GC Biopharma

WHO Prequalified Seasonal Influenza Vaccines[2]

Prequalified	Type	Commercial Name	Pharmaceutical Form	Presentation	No. of Doses	Manufacturer
12/04/2011	Influenza, seasonal (Trivalent)	**GCFLU inj.**	Liquid: ready to use	Vial	1	GC Biopharma
07/11/2012	Influenza, seasonal (Trivalent)	**GCFLU Multi inj.**	Liquid: ready to use	Vial	10	GC Biopharma
21/12/2016	Influenza, seasonal (Quadrivalent)	**GCFLU Quadrivalent inj.**	Liquid: ready to use	Vial	1	GC Biopharma
03/04/2017	Influenza, seasonal (Quadrivalent)	**GCFLU Quadrivalent Multi inj.**	Liquid: ready to use	Vial	10	GC Biopharma

- WHO prequalification ensures vaccines used in immunization programmes are safe and effective. [3]
- It provided Member States and procurement agencies, such as UNICEF. [3]
- Once a vaccine is prequalified and introduced to the market, WHO ensures it continues to meet standards. [3]

GC FLU Quadrivalent Pre-filled Syringe inj.

GC Biopharma

Seasonal Influenza

Influenza and its complications have a large social impact including increased demands on the healthcare system and patient disability and mortality. [4]

[WHO's annual estimates about seasonal influenza [5]]

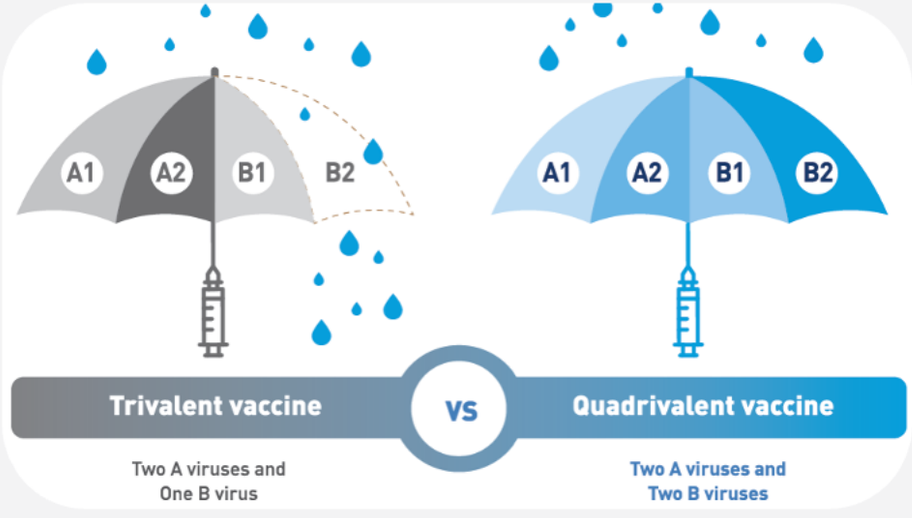
3-5 million cases
of severe illness

290,000-650,000
respiratory deaths

Influenza Vaccine

The most effective way to prevent the disease is vaccination. [5]
Although hospitalization and death were most common from influenza A/H3N2, the number of hospitalizations and deaths from influenza B was higher than that of seasonal influenza A/H1N1 before the 2009 pandemic. [6]

55.6 % of circulating B viruses were mismatched
During influenza seasons from 2007 to 2014[7]



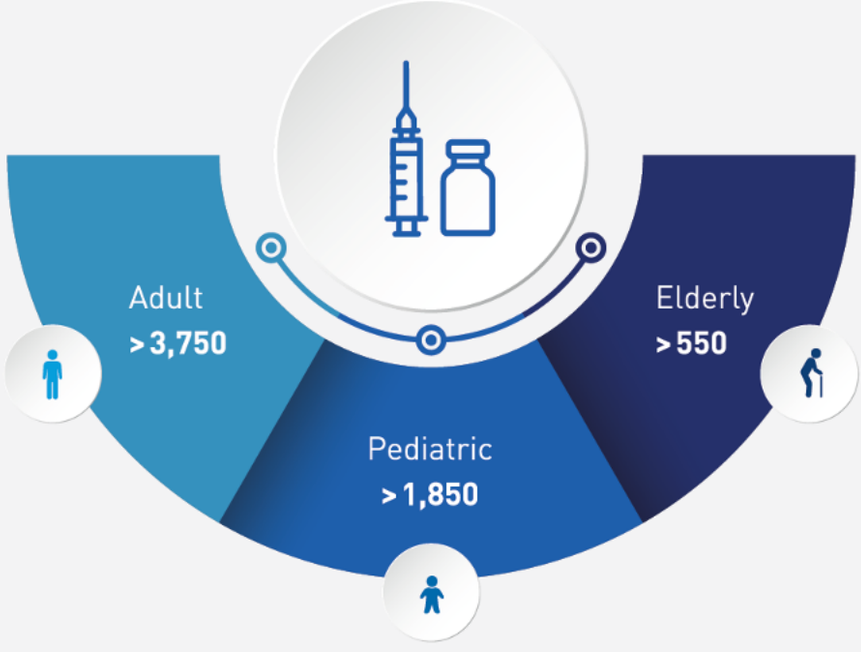
Quadrivalent vaccine include a 2nd influenza B virus in addition to the viruses in trivalent vaccines, and are expected to provide wider protection against influenza B virus infections. [5]

GC FLU Quadrivalent
Pre-filled Syringe inj.

GC Biopharma

Clinical Studies of GCFLU TIV

Clinical studies have been conducted to examine the immunogenicity and safety of GCFLU TIV,
GCFLU TIV showed excellent immunogenicity and good tolerability in clinical studies involving ~6,200 subjects. [8]



Young Children with Recurrent Wheezing

Especially in infancy, wheezing frequently is associated with respiratory viral infections and allergy; about 20% of these children have recurrent wheezing episodes and might become asthmatic patients.

Patients with Rheumatoid Arthritis

Patients with RA are more susceptible to infections because of their underlying immune dysfunction and the treatment-induced immune suppression.

Cancer Patients

Cancer patients receiving cytotoxic chemotherapy are at increased risk of being infected with the influenza virus.

GC FLU Quadrivalent Pre-filled Syringe inj.

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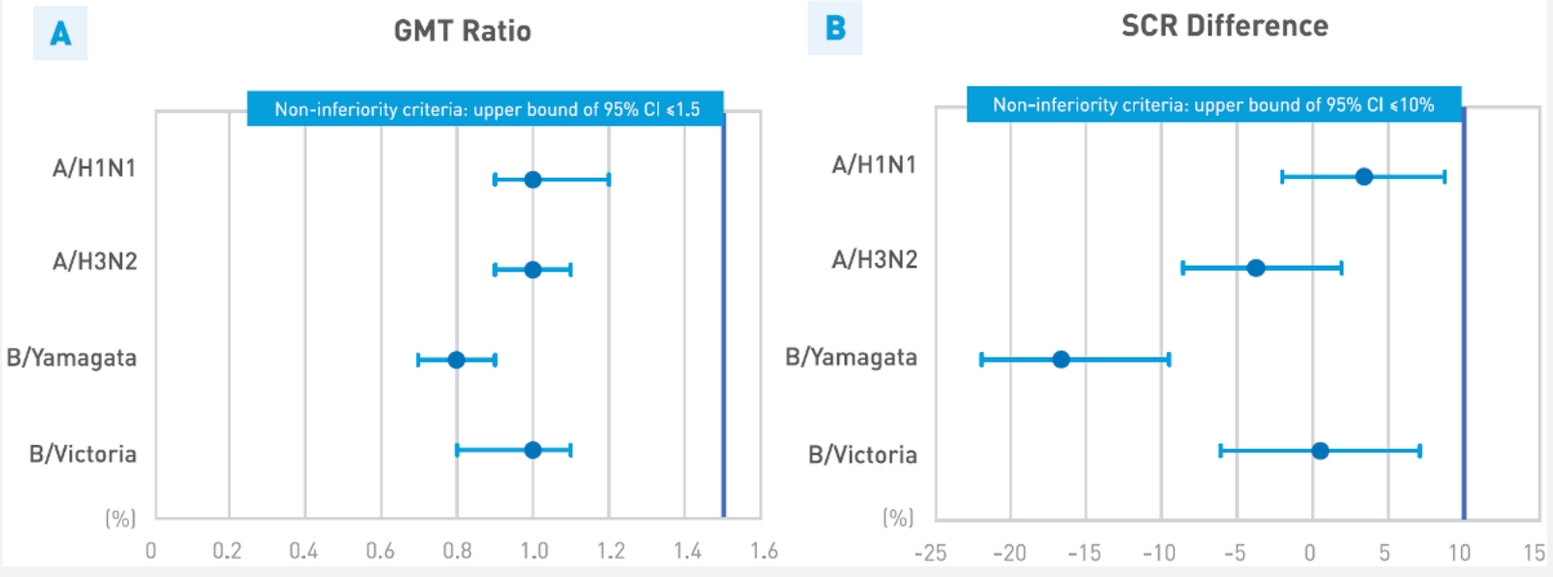
GCFLU QIV: Immunogenicity in Adults

GCFLU QIV, compared to the control GCFLU TIV, met the non-inferiority criteria* for all four-influenza subtype/ lineage strains with respect to GMT ratio and SCR difference in subjects ages ≥ 19 years. [6]

[Post-vaccination non-inferiority analysis of (A) GMT ratio and (B) SCR difference [6]]



*For non-inferiority, the following criteria should be met: (!) the upper bound of the two-sided 95% CI of the GMTRs (TIV/QIV) for all four vaccine strains should not exceed 1.5, and (2) the upper bound of the two-sided 95% CI for the SCR difference (TIV minus QIV) for all four vaccine strains should not exceed 10%.

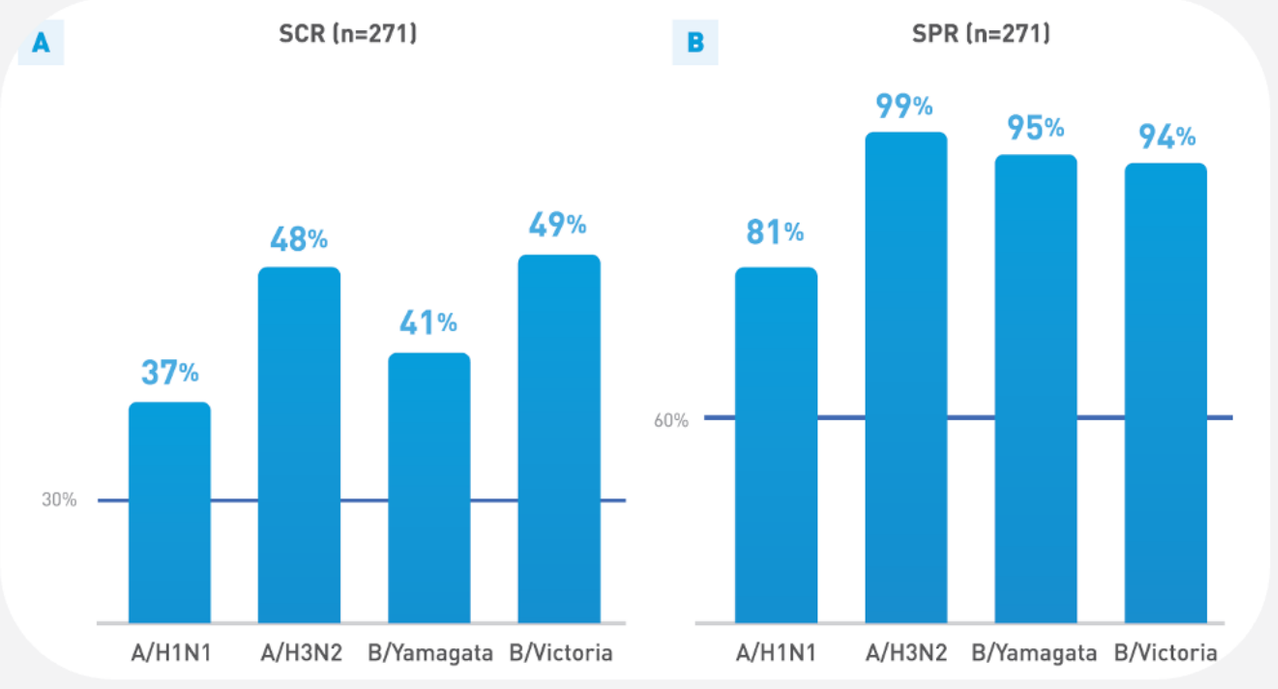
GC FLU Quadrivalent Pre-filled Syringe inj.

GC Biopharma

GCFLU QIV: Immunogenicity in Adults aged ≥ 65 years

GCFLU QIV induced immunogenicity that met the MFDS standards* in healthy subjects aged ≥ 65. [14]

[SCR (A) and SPR (B) in adults ages ≥ 65 [14]]



*Standards (criteria) for adults aged ≥ 65 years: [SCR] lower bound of 95% CI ≥30%, [SPR] lower bound of 95% CI ≥60% CI, confidence interval; SCR, seroconversion rate; SPR, seroprotection rate; QIV, quadrivalent influenza vaccine

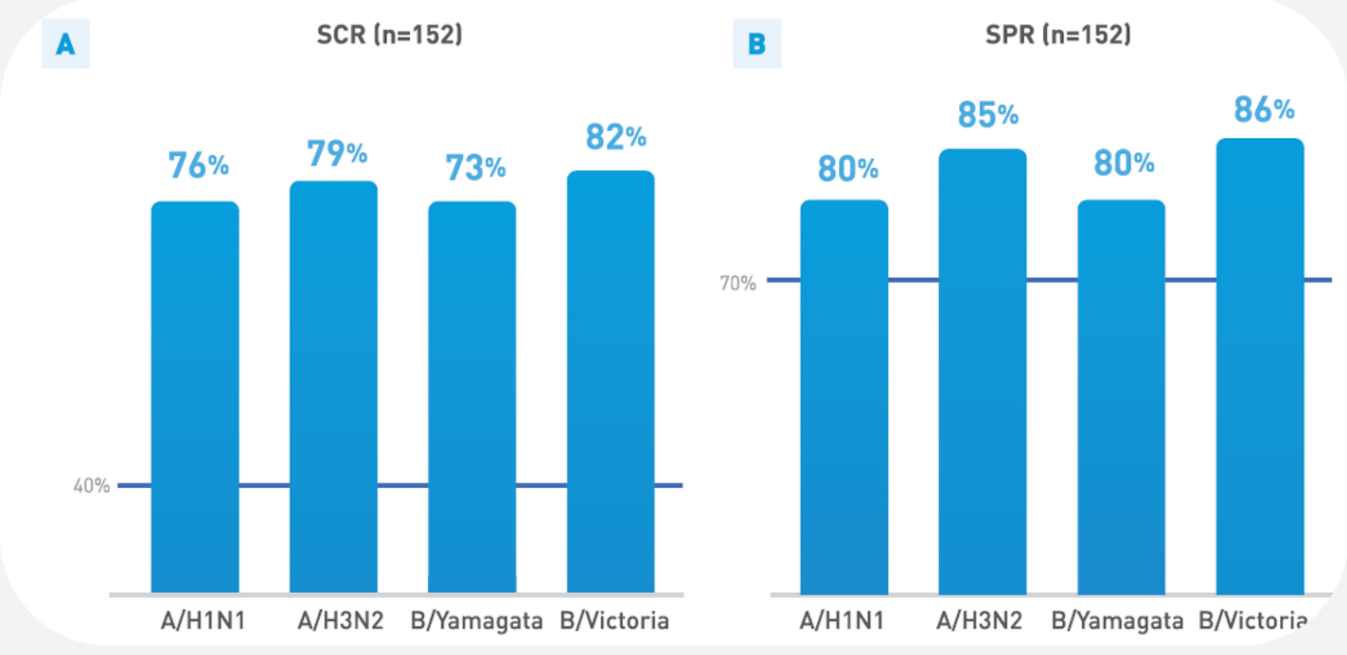
GC FLU Quadrivalent Pre-filled Syringe inj.

GC Biopharma

GCFLU QIV: Immunogenicity in Children aged ≥ 6 months to < 3 years

GCFLU QIV induced immunogenicity that met the MFDS standards* in children ages ≥ 6 months to < 3 years. [15]

[SCR (A) and SPR (B) in aged ≥ 6 months to < 3 years [15]]



*Standards (criteria) for children ages ≥ 6months to < 3 years' [SCR] lower bound of 95% CI ≥ 40%, [SPR] lower bound of 95% CI ≥ 70%

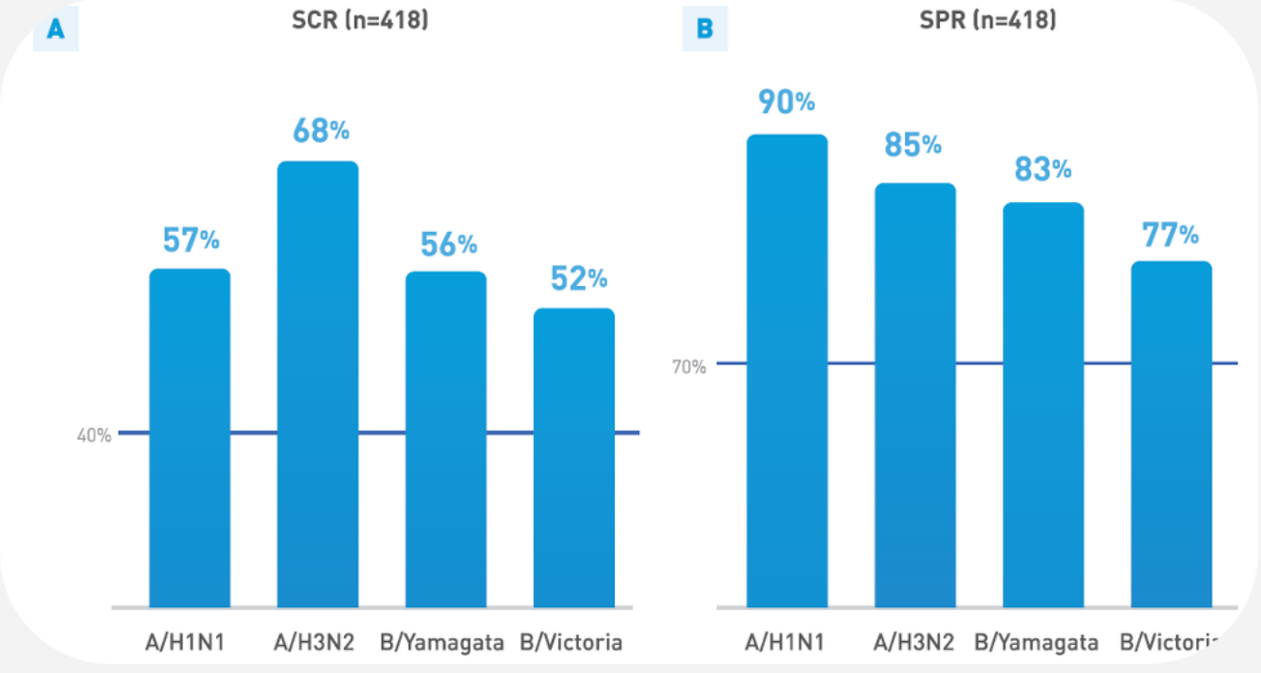
GC FLU Quadrivalent Pre-filled Syringe inj.

GC Biopharma

GCFLU QIV: Immunogenicity in Children and Adolescents

GCFLU QIV induced immunogenicity that met the criteria* and broader protection to children and adolescents aged ≥ 6months to < 19 years than the GCFLU TIV. [16]

[SCR (A) and SPR (B) in children aged ≥ 6 months to < 19 years [16]]



*Criteria for children and adolescents Age ≥ 6 months to < 19 years; [SCR] lower bound of 95% CI ≥ 40% [SPR] lower bound of 95% CI ≥ 70% CI, confidence interval; SCR, seroconversion rate; SPR, seroprotection rate; QIV, quadrivalent influenza vaccine

GC Biopharma

I.V.-Globulin SN inj.

Human Normal Immunoglobulin for
Intravenous Administration

GC Biopharma

I.V.-Globulin SN inj.

High Safety

Qualified Donors

Plasma used for manufacture of I.V.-Globulin SN inj. is collected from eligible donors obtained from FDA licensed centers located in the U.S..

Plasma Testing

In order to assure the safety we retest all receiving plasma units from plasma suppliers in accordance with International Regulation.
Tests are performed by using sensitive diagnostic kits (Anti-HIV 1/2, HBsAg, Anti-HCV) prior to manufacturing.

Manufacturing

3-step virus inactivation/removal process : Fraction III Precipitation S/D virus inactivation Nano-Filtration

The sterile 5% IgG solution is manufactured according to the Cohn-Oncley cold ethanol fractionation process followed by chromatographic purification. The manufacturing process includes specifically designed virus inactivation/removal steps called S/D treatment and Nano-Filtration.
The product is stabilized with 10% maltose. The formulation contains no preservatives.

Our 3-step Virus Inactivation Process

We use three different virus inactivation/elimination steps to ensure safety of our product.

GC Biopharma

I.V.-Globulin SN inj.

High Quality

Virus Validation

Using designed lab scale model, virus validation studies were performed. The materials used in validation studies were taken from actual process intermediates.

Summary of results are presented in below table.

	Enveloped virus				*Non-enveloped virus*	
Target virus	HIV	HBV	HBV	HCV	HAV	B19
Model virus	HIV-1	BHV	PRV	BVDV	HAV	PPV
Fraction II precipitation	≥ 4.97	≥ 6.22	N/T	≥ 4.21	≥ 4.11	3.53
S/D treatment	≥ 4.78	N/T	≥ 5.32	≥ 4.83	N/A	N/A
Nano-Filtration	≥ 5.99	N/T	≥ 5.59	≥ 5.56	≥ 4.46	6.62
Cumulative LRF	≥ 15.74	≥ 6.22	≥ 10.91	≥ 14.26	≥ 8.57	10.15

HIV (Human Immunodeficiency virus) **HBV** (Hepatitis B virus) **HCV** (Hepatitis C virus)
HAV (Hepatitis A virus) **B19** (Human parvovirus B19)
BHV (Bovine herpes virus) **PRV** (Pseudorabis virus) **BVDV** (Bovine viral diarrhea virus)
PPV (Porcine parvovirus) **LRF** (Log reduction factor(log 10))
N/T (Not tested) **N/A** (Not applicable)

I.V.-Globulin SN inj. is SAFE against Thrombogenic Effect

1) Wesseler Test

Wesseler test results showed that I.V.-Globulin SN inj., each at dose levels of 500, 1,000 or 2,000 mg/kg b.w. did not show any thrombogenic effect.

2) TGA

Thrombin generation assay of I.V.-Globulin SN inj. and competitor products is presented in below table.

Manufacturing Firm	*Thrombin (nM)*	*FXIa (pM)*
GCC	155.0	28.3
Company A	184.8	32.3
Company B	151.2	24.5
Company C	226.5	50.2
Company D	169.2	28.2

I.V.-Globulin SN inj. showed only a minimal increase in thrombin generation and had no effect on factor XIa-deficient plasma as same as other competitor products.

GC Biopharma

I.V.-Globulin SN inj. Human Normal Immunoglobulin for Intravenous Administration

[DESCRIPTION]

'I.V.-Globulin SN inj. (Human Normal Immunoglobulin in maltose, pH 4.25)' is a biological product, manufactured with plasma from individual donors. Manufacturing processes include thawing, cold ethanol fractionation, and virus inactivation, such as S/D treatment and nano-filtration. The following manufacturing processes are applied in order to produce a finished product. Firstly, fraction II which comes from fractionated plasma is purified with chromatography, and S/D treatment is applied for the virus inactivation. Additional purification processes include dia-filtration, and is performed accordingly.

[QUANTITATIVE COMPOSITION]

1 mL contains,

Human Immunoglobulin-G (active ingredient) ---------- 50 mg

Maltose (stabilizer) ---------- 100 mg

Water for Injection (solvent) ---------- q.s.

[CLINICAL PARTICULARS]

1. Therapeutic indications

1) A-/Hypogammaglobulinemia

2) Combined therapy with antibiotics in severe bacterial or viral infections

3) Idiopathic Thrombocytopenic Purpura (In the case where other medicinal products are not effective or patients show apparent hemorrhage or patients need temporary control of hemostasis such as surgeon treatments or childbirth etc.)

4) Guillain-Barre Syndrome (Subacute febrile polyneuritis)

5) Kawasaki Syndrome (To prevent the disease of coronary artery complication)

2. Posology and method of administration

1) For combined therapy with antibiotics in severe bacterial or viral infections and A-Hypogammaglobulinemia, the usual dosage for adults and children is 2,500~5,000 mg and 50~150 mg/kg respectively(as a single dose) by intravenous drip infusion or direct intravenous infusion. In case of intravenous injection, it should be injected very slowly.

2) Idiopathic Thrombocytopenic Purpura (ITP): The usual dosage for the treatment of acute or chronic ITP is 200-400 mg/kg daily given for 5 consecutive days. The additional doses are discontinued if an adequate response does not occur.

3) Guillain-Barre Syndrome: The usual dosage is 400 mg/kg daily given for 5 consecutive days.

4) Kawasaki Syndrome: The usual dosage is 400 mg/kg daily given for 5 consecutive days (approximately), or 2,000mg daily by intravenous drip infusion. It is recommended that the administration of I.V.-Globulin SN inj. start after 7 days from the onset of Kawasaki Syndrome.

3. Contraindications

1) Patients with history of anaphylaxis to ingredients of I.V.-Globulin SN inj.

2) Patients with history of shock to ingredients of I.V.-Globulin SN inj.

4. Special warnings and precautions for use

(1) Special warnings

1) I.V.-Globulin SN inj., manufactured from human plasma, has the potential to transmit hepatitis viruses or other viruses which can cause infection. The risk of virus infection cannot be entirely eliminated. Accordingly, patients with hemophilia or immunodeficiency are recommended to be appropriately vaccinated (Hepatitis A vaccine, etc.), and the attending physician should monitor patients regularly to check any sign of virus infection. Since I.V.-Globulin SN inj. has potential risks as described above, the product must be carefully used. If the product is prescribed, only the necessary amount should be administered.

2) The risk of thrombosis by administration of this product cannot be entirely eliminated. Thrombosis may occur regardless of the route of administration and in the absence of known risk factors (advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling central vascular catheters, hyperviscosity and cardiovascular risk factors). For patients at risk of thrombosis, administer at the minimum concentration possible and at the minimum rate of infusion practicable. Also ensure adequate hydration in patients before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity.

(2) Special precautions

1) Patients with IgA deficiency (I.V.-Globulin SN inj. may cause anaphylaxis to patients who have anti-IgA)

2) Patients with renal disorder (Renal function may deteriorate.)

3) Patients with hemolytic anemia or anemia from blood loss (Human parvovirus B19 infection may occur. In case of B19 infection, acute systemic symptoms with fever and severe anemia may occur.)

4) Patients with immunological incompetence or immunodeficiency (Human parvovirus B19 infection may occur. In case of infection, continuous anemia may occur.)

5) Patients with cerebrovascular and cardiovascular disorders or case history thereof for example, elderly patients with ischemic disease, cardiovascular disorder, cerebrovascular disorder. (A large bolus administration can cause thrombus or embolism such as cerebral infraction, a myocardial infraction, etc due to blood viscosity increase.)

6) Patients with high risk of thrombus or embolism (Thrombus or embolism may occur due to an increase of blood viscosity due to large bolus administration.)

7) Patients with low heart function (A large bolus administration may cause heart failure or deterioration of heart condition)

(3) General cautions

1) In case of successive or interval administration, shock or severe abnormal reactions may occur. Accordingly, administration should be done with caution, and catamnesis also should be carefully observed. Especially for children, special caution should be taken for the rate of administration and catamnesis.

2) Administration of I.V.-Globulin SN inj. for the treatment of Idiopathic Thrombocytopenic Purpura is for symptomatic therapy, not causal treatment.

3) In case of Idiopathic Thrombocytopenic Purpura for children, spontaneous remission should be considered.

4) In present plasma fractionation process, it is difficult to inactivate or remove human parvovirus B19, etc. completely. Accordingly, possibilities of infection cannot be disregarded, and special caution should be taken for catamnesis.

5) Even though a safety plan for the prevention of the spread of infection is prepared, the risk of infection cannot be entirely disregarded since I.V.-Globulin SN inj. originates from human blood. This risk should be explained to patients.

6) Since I.V.-Globulin SN inj. contains anti-A and anti-B, hemolytic anemia may occur when a large bolus is administered to patients with blood type A, B or AB.

7) Additional administration to patients with Kawasaki Syndrome should be conducted when the effectiveness of I.V.-Globulin SN inj. is insufficient (e.g. symptomatic remission) or additional administration is clearly necessary. (Safety and efficacy for additional administration has not been established)

8) In the case of combined therapy with antibiotics in severe infections, I.V.-Globulin SN inj. should be used for patients who show insufficient response to proper antimicrobial chemotherapy.

9) There have been published reports that immune globulin intravenous injection is related to disorders of renal function, osmotic renal diseases including death, etc.

10) Patients should be aware of the risk and discuss with their healthcare professionals and contact them if any signs or symptoms of thrombosis during or after receiving this product develop. Signs or symptoms of thrombosis may include pain and/or swelling of an arm or leg with warmth over the affected area, discoloration of an arm or leg, unexplained shortness of breath, chest pain or discomfort that worsens on deep breathing, unexplained rapid pulse, chest pain and numbness or weakness on one side of the body.

11) Healthcare professionals should be aware of the risk for thrombosis with human normal immunoglobulin products and discuss with their patients the risk of thrombosis associated with this product. Monitor patients carefully for signs and symptoms of thrombosis both at the time of infusion and after infusion and encourage patients to report any signs or symptoms.

osmotic renal diseases including death, etc.

5. Interaction with other medicinal products and other forms of interaction

There is a possibility that live vaccines (Measles, Mumps, Rubella, Varicella vaccine, etc.) do not work for the patients who were treated with I.V.-Globulin SN inj.. Therefore, vaccination should be delayed for 3 months after administration.

If I.V.-Globulin SN inj. is administered within 14 days after vaccination, re-vaccination should be taken after more than 3 months post I.V.-Globulin SN inj. administration. After a large bolus (more than 200mg/kg) administration for the ITP and Kawasaki disease, use of live vaccines should be delayed more than 6 months (In case of low risk of measles infection, measles vaccination can be delayed more than 11 months).

6. Pregnancy and lactation

Safety for a pregnant woman has not been established. The possibility of parvovirus B-19 infection cannot be excluded from the administration of I.V.-Globulin SN inj. In case of parvovirus B-19 infection, fetal disturbances (abortion, hydrops fetalis, fetal death) may occur. I.V.-Globulin SN inj. should be given to a pregnant woman only if the expected benefit justifies the possible risk.

7. Pediatric use

Safety for low birth weight infants and neonates has not been established.

8. Geriatric use

Since elderly patients generally have low physiological function, I.V.-Globulin SN inj. should be administered with special care.

9. Influences to clinical examination results

I.V.-Globulin SN inj. contains pathogens or antibodies against the pathogens. Therefore, antibodies can be occasionally detected in blood after administration. Clinical diagnosis should be taken with special cautions and confirmed.

10. Effects on ability to drive and use machines

Some of the effects mentioned under section 11 "Undesirable Effects" may affect the ability to drive or use machines.

11. Undesirable Effects

1) Shock: Symptoms of shock may occur. If dyspnea, wheeze, chest pain, hypotension or weak pulse are watched, administration should be discontinued, and 0.1~0.5 mL epinephrine (1:1,000) or the administration of cortisone should be considered.

2) Circulatory: Rapid administration can cause hypotension. (Caution should be taken to patients with A-/Hypogammaglobulinemia.)

3) Liver: Liver function disorders or jaundice accompanying and increase in ALT or AST may occur. Caution should be taken, and proper treatment should be followed if needed.

4) Kidney: It has been reported in the literature that acute renal failure may occur with the use of immune globulin (human) products. If dehydration, hypouresis, increase of creatinine or increase of BUN, etc. are observed, administration should be discontinued, and proper treatment should be taken.The administration dosage and rate should be lowered (as low as possible) for patients at high risk patients for acute renal failure.

5) Central Nervous System: Aseptic meningitis from a large volume of I.V.-Globulin SN inj. administration (Nuchal rigidity, fever, headache, nausea, vomiting, mental fog, etc.) may occur. In these cases, administration should be discontinued and proper treatment taken.

6) Blood: Because a decrease in platelets may occur with the administration of I.V.-Globulin SN inj., caution should be taken. If this symptom occurs, proper treatment should be taken.

7) Other possible undesirable effects: Drowsiness, chill, chest pain, abdominal pain, gluteal pain and anxiety may occur in rare cases.

12. Incompatibilities

In the absence of compatibility studies, this medical product must not be mixed with other medicinal products.

[SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING]

1. Precautions for administration

1) Avoid mixing with other medicinal products except for 5%-Glucose. (Do not mix with normal saline)

2) Rapid administration may cause hypotension. Drip infusion intravenous injection is recommendable. If direct intravenous injection is needed, it should be administered very slowly. (Caution should be taken with A-/Hypogammaglobulinemia patients.)

3) If particulate matter is observed, or color is not clear, the product should be discarded.

4) I.V.-Globulin SN inj. should be used within 1 hour after the container is opened. Do not use the remaining solution due to the possibility of microbial contamination. (I.V.-Globulin SN inj. is protein and does not contain preservatives.)

5) Do not use if I.V.-Globulin SN inj. was ever frozen.

2. Precautions for handling

When a needle is inserted through the rubber stopper, the needle should be inserted vertically and slowly. If a needle is inserted in a tilted or twisted direction, rubber fragments may be mixed with medicinal product. If there are any rubber fragments, discard the product.

[SHELF-LIFE] 30 months from the manufacturing date.

[STORAGE] Store at 2~8°C in hermetic container. Store in a dark place.

[HOW SUPPLIED] 10 ml (500 mg) / 20 ml (1,000 mg) / 50 ml (2,500 mg) / 100 ml (5,000 mg) / 200 ml (10,000 mg)

Hunterase

Idursulfase-ß

GC Biopharma

Hunterase Idursulfase-β

Enzyme Replacement Therapy for MPS II (Hunter syndrome)

GC Biopharma

Serum-Free Production Process

Reduced risk of pathogen contamination (Mycoplasmas, Viruses, Prions, etc.)

Effective Viral Inactivation and Removal Steps

(Low pH Inactivation & Nanofiltration - Dual Clearance)
Improved safety against potential enveloped and non-enveloped virus contamination

High Proportion of Active-Form Enzymes

High level of formylglycine-form peptides (79.40±0.92%)

Hunter Syndrome (Mucopolysaccharidosis II)

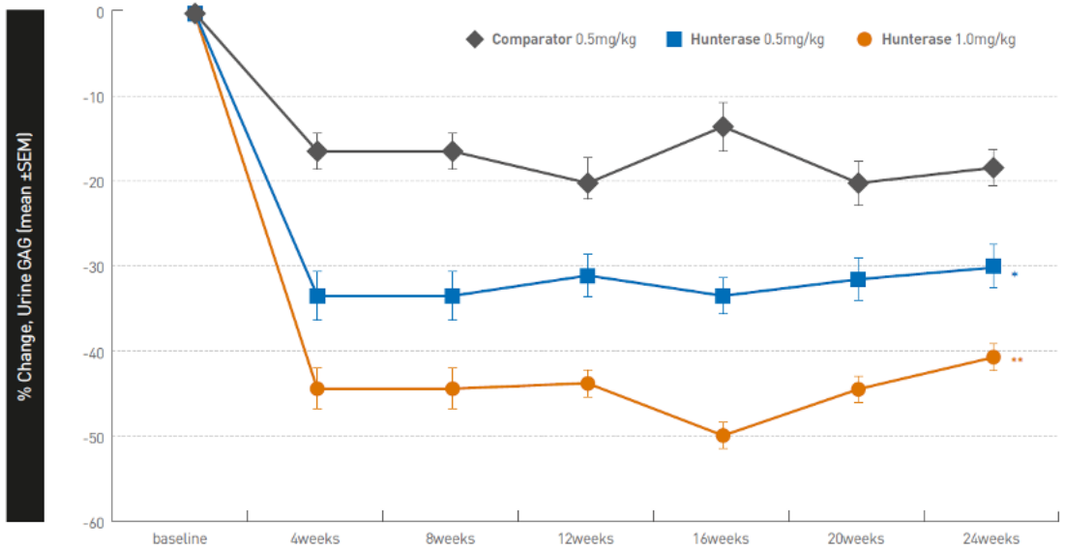
Hunter Syndrome (Mucopolysaccharidosis II; MPS II) is a rare X-linked lysosomal storage disorder caused by the deficiency of iduronate-2-sulfatase (IDS). In affected patients, glycosaminoglycans (GAGs) accumulate in the lysosomes of many organs and tissues contributing to the pathology associated with MPS II.
The common symptoms and signs include developmental delay, coarse face, short stature, skeletal abnormalities (dysostosis multiplex), joint contracture, hepatosplenomegaly, upper airway obstruction, and valvular heart disease.1)

Hunterase Idursulfase-ß

Enzyme Replacement Therapy for MPS II (Hunter syndrome)

GC Biopharma

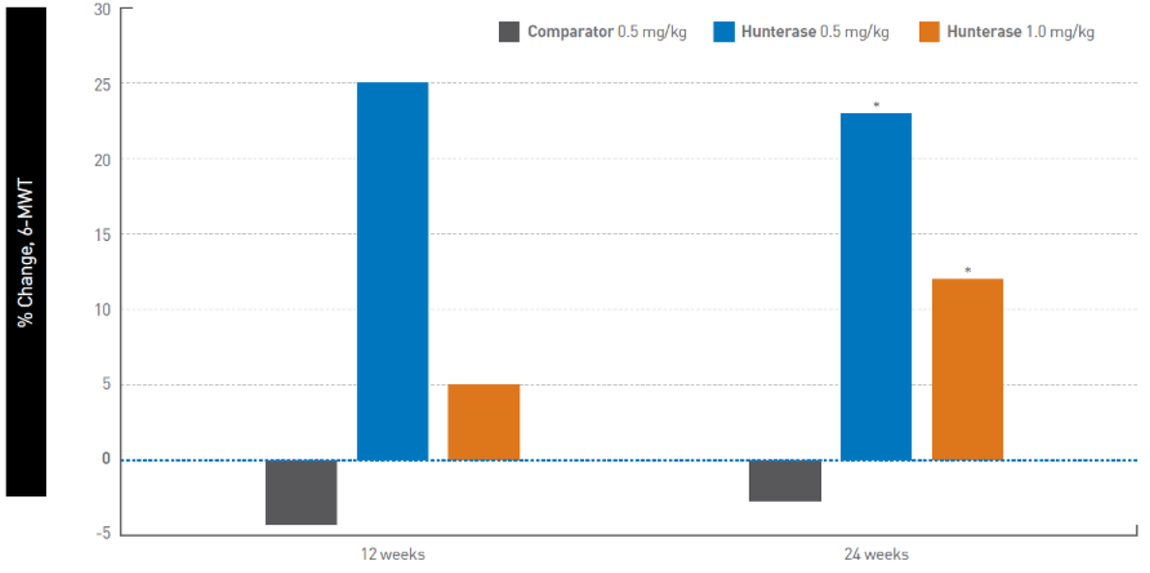
Hunterase reduced urinary GAG[1)]



(Mean ± SEM) * ANCOVA(<0.05, significant difference vs. comparator), Covariate: Age Group, Hunter Syndrome Severity
** ANCOVA(<0.01, significant difference vs. comparator), Covariate: Age Group, Hunter Syndrome Severity

Hunterase treatment resulted in a significant reduction in urinary GAG excretion in patients with MPS II.

Hunterase improved 6MWT distance[1)]



* P<0.05 (vs. comparator, T-test)

Hunterase treatment resulted in an improvement in the 6MWT distance.

Hunterase Idursulfase-ß
Enzyme Replacement Therapy for MPS II (Hunter syndrome)

GC Biopharma

Hunterase demonstrated an acceptable safety profile[7)]

	Comparator	Hunterase	
	0.5 mg/kg (N=11)	0.5 mg/kg (N=10)	1.0 mg/kg (N=10)
	n (%) [case]	n (%) [case]	n (%) [case]
Safety Population	11	10	10
Adverse Drug Reactions	2 (18.2%) [19]	1 (10%) [4]	2 (20%) [3]
Skin and Subcutaneous Tissue Disorders	2 (18.2%) [18]	1 (10%) [3]	2 (20%) [3]
General Disorders and Administration Site Conditions	-	1 (10%) [1]	-
Respiratory, Thoracic and Mediastinal Disorders	1 (9.1%) [1]	-	-

Hunterase treatment was well tolerated in patients with MPS II. All of the ADRs were mild and easily controlled with an adjustment of the infusion rate or medications.

No newly detected antibodies after Hunterase administration[1)]

Group	No. of Positive Subjects before the Treatment (Baseline)	No. of Positive Subjects after 24 Weeks
Comparator 0.5 mg/kg	4	4
Hunterase 0.5 mg/kg	4	4
Hunterase 1.0 mg/kg	2	2

The results of antibody screening tests were the same as the baseline results.

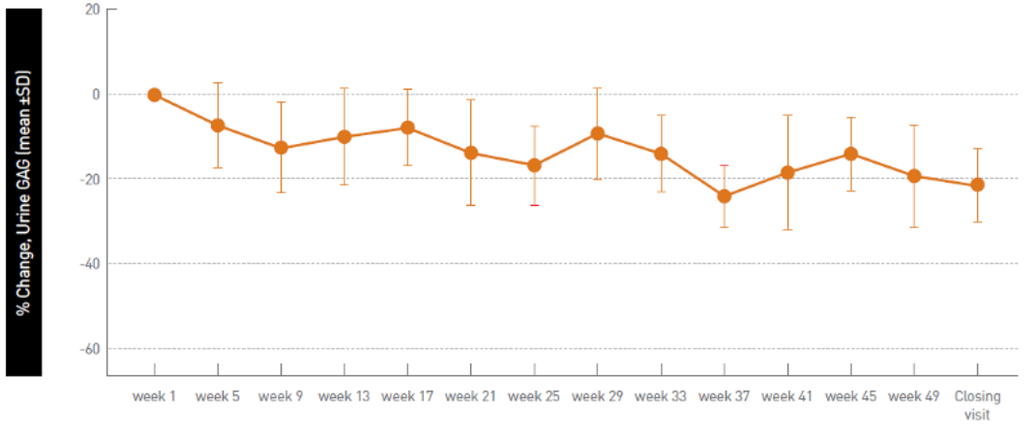
Hunterase Idursulfase-ß
Enzyme Replacement Therapy for MPS II (Hunter syndrome)

GC Biopharma

Pediatric Study of Hunterase[6)]
(for patients under the age of six)

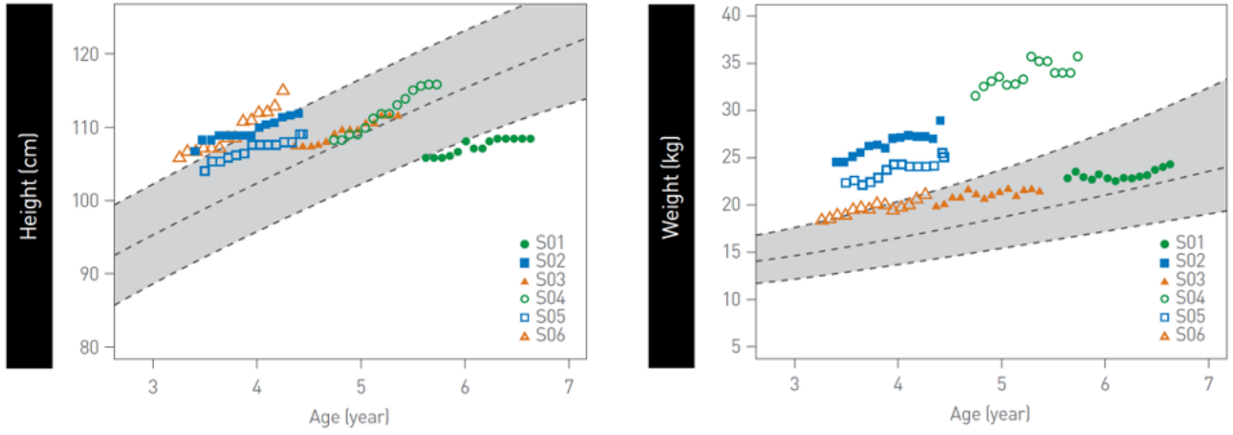
The pediatric study results indicate that the safety and efficacy of Hunterase are similar to those reported in Hunter syndrome patients aged 6 years or older.

Reduction of Urine GAG



The treatment of Hunterase(0.5 mg/kg/week) in patients under 6 years of age significantly reduced urine GAG by -35.1 ± 30.6 mg GAG/g creatine at week 53 (P=0.038) from baseline.

The Growth Chart for Each Patient



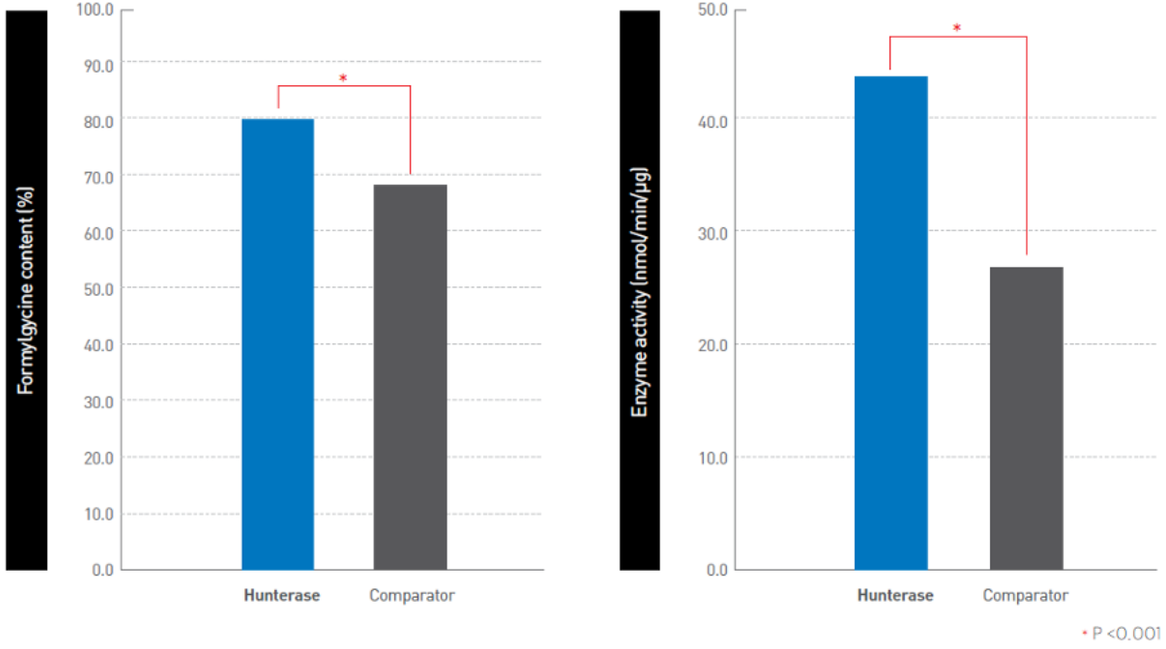
Height and weight of the patients were significantly increased at week 53 (P = 0.002 and P = 0.003, respectively).
Significant increases in height and weight observed during the study were regarded as normal growth velocity in this age population.
※The dotted lines in the graphs represent 5th, 50th, 95th percentiles of standard growth curve of normal Korean boys, respectively.

Hunterase Idursulfase-ß
Enzyme Replacement Therapy for MPS II (Hunter syndrome)

GC Biopharma

High formylglycine (FGly) content of Hunterase[5)]

Comparison of FGly Content and Enzyme Activity between Hunterase and the comparator.



* P <0.001

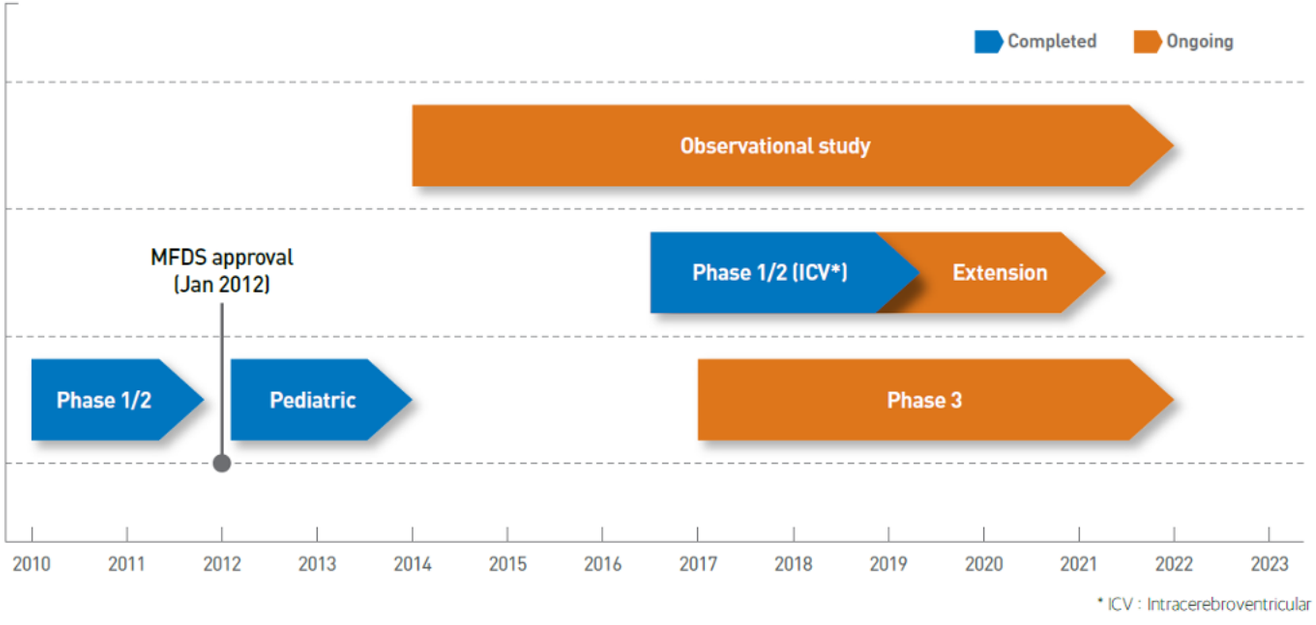
The FGly content determines the enzyme activity.

	Hunterase	Comparator
FGly content	**79.40 ± 0.92%**	68.12 ± 2.22%
Enzyme activity (substrate degradation, 4-MU)	**42.58±1.11 nmol/min/μg**	27.76±0.94 nmol/min/μg
Cell uptake (normal human fibroblasts)	**5.09 ± 0.96 nM**	6.50 ± 1.28 nM

Hunterase Idursulfase-ß
Enzyme Replacement Therapy for MPS II (Hunter syndrome)

GC Biopharma

Clinical trials of Hunterase



* ICV : Intracerebroventricular

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7) Clinical Study Report for Hunterase Phase I/II trial. GC Pharma. 2012

GC Biopharma

Hunterase

ICV Injection 15 mg

World's 1st approved treatment
for Neuronopathic MPS II

Hunterase ICV Injection 15 mg

Enzyme Replacement Therapy for MPS II (Hunter syndrome)

GC Biopharma

Signs & Symptoms1, 2)

66.7% neuronopathic

33.3% non-neuronopathic

Neuronopathic (severe) type : CNS involvement

Neurobehavioral symptoms

- Aggression
- Sleep disturbances
- Cognitive impairment
- Hyperactivity
- Progressive neurological decline

Non-neuronopathic (attenuated) type : Minimal CNS involvement

Common symptoms & signs

- Developmental delay
- Short stature
- Coarse face
- Skeletal abnormalities (dysostosis multiplex)
- Joint contracture
- Upper airway obstruction
- Hepatosplenomegaly
- Valvular heart disease

Early Diagnosis and Prescription are Keys to Better Outcomes

Hunterase ICV Injection 15 mg

Enzyme Replacement Therapy for MPS II (Hunter syndrome)

GC Biopharma

Unmet needs in IV ERT-treated patients

1 Symptoms of CNS involvement[3]

Since conventional intravenous enzyme replacement therapy (ERT) does not reach the brain compartment due to the **Blood brain barrier (BBB),** the abnormal accumulation of glycosaminoglycans in the brain can lead to degeneration of brain tissue and progressive decline in cognitive function. Cognitive development stops at the age of 3-4 years and regression starts at the age of 4-5 years.

3 Life Expectancy[5,6]

The life expectancy of MPS II patients can depend on the severity of their condition. In severe cases of MPS II, life expectancy is significantly reduced and **may be limited to the teenage years or early adulthood** compared to a longer the life expectancy until the fifth or sixth decade in the attenuated type. Eearly diagnosis and intervention are indeed critical in prolonging life expectancy and improving the quality of life as well.

2 Quality of Life[4]

In the neuronopathic type of MPS II, developmental age can be significantly affected by the CNS involvement associated with the disorder. The patients experience **intellectual disabilities and delays in speech and language development,** which can affect their ability to learn, communicate, and function independently. In addition, the progressive nature of MPS II can lead to a decline in physical abilities over time, including difficulties with fine motor skills and mobility. These factors can further affect an individual's developmental age and overall quality of life.

Hunterase ICV Injection 15 mg

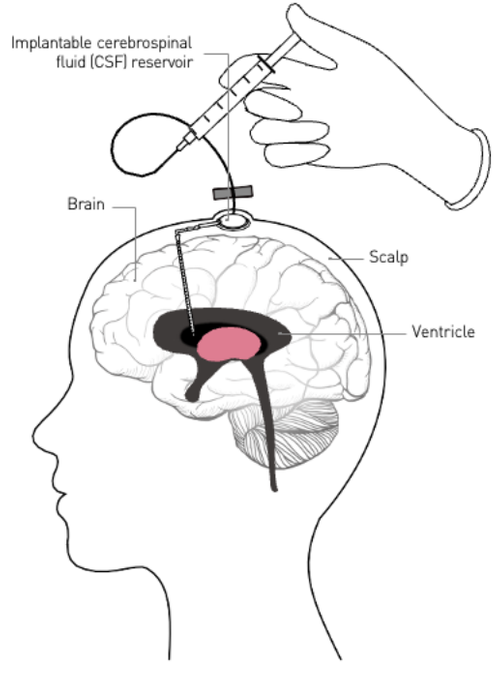
Enzyme Replacement Therapy for MPS II (Hunter syndrome)

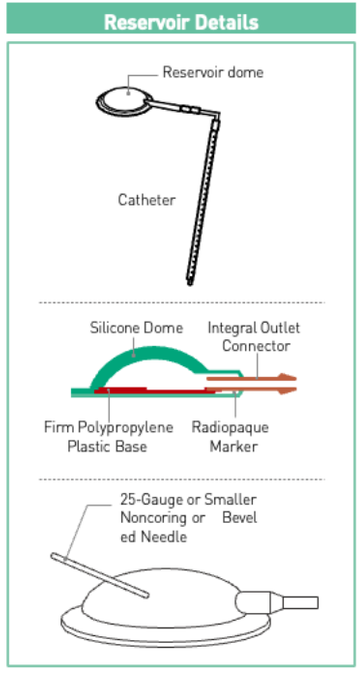
GC Biopharma

Novel ERT with ICV administration of Hunterase ICV inj.

- World's 1st product developed for Neuronopathic MPS II
- Approved by PMDA, Japan (2021)
- High-dosage formulation (15 mg/ml) and with a long dosing interval (1q4W)
- Administered over at least 1 minute
- Generally well tolerated for the neuronopathic MPS II
- Reduces GAG concentrations in the CSF and prevents and stabilizes developmental decline
- 4+ years of experience in Japan including clinical trials

"Hunterase ICV inj. is directly delivered to the cerebral ventricle using an implanted CSF reservoir"





Hunterase ICV Injection 15 mg

Enzyme Replacement Therapy for MPS II (Hunter syndrome)

GC Biopharma

Clinical trial

Study design and objectives

A multicenter, open-label, phase 1/2 clinical study was conducted to evaluate the efficacy and safety of ICV idursulfase-β in patients with MPS II. ICV Idursulfase-β (increasing from 1 to 30 mg between weeks 0 and 24, followed by a 30-mg final dose) was administered intracerebroventricularly once every 4 weeks using an implanted cerebrospinal fluid (CSF) reservoir; intravenous (IV) administration of idursulfase was also continued throughout the study.

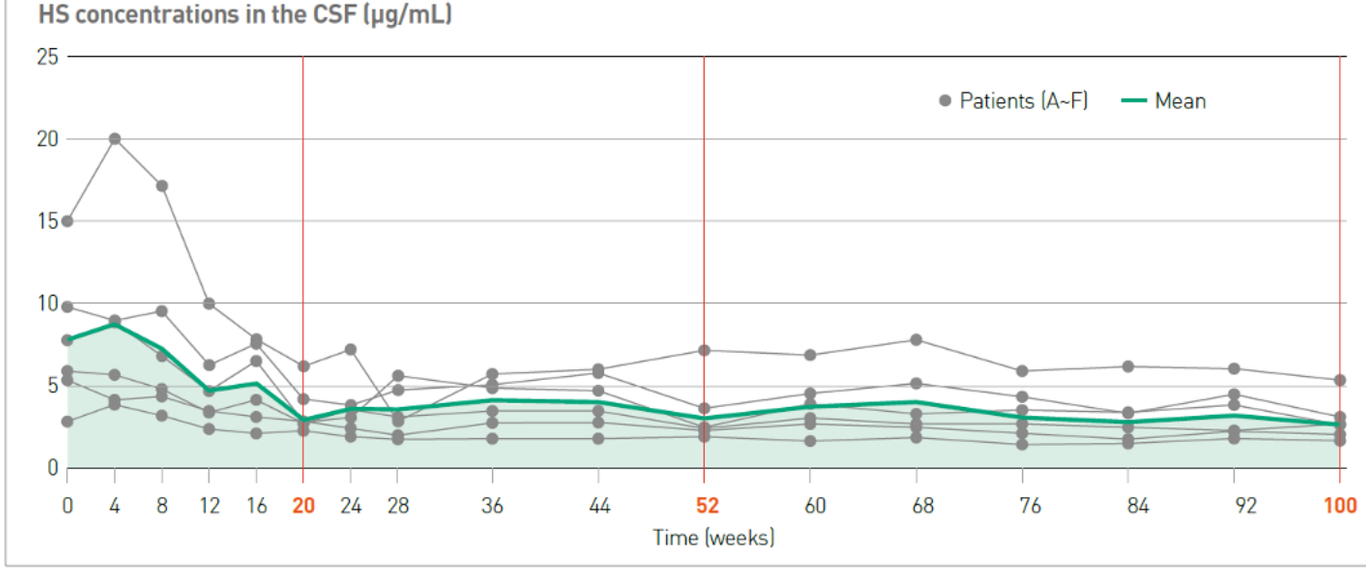
Primary endpoint

Heparan sulfate (HS) concentration in the CSF.

Results

Intracerebroventricular (ICV) administration of idursulfase-β decreased HS concentrations in the CSF by 40% - 80% from baseline to week 100 in all six patients.

Change in HS in the CSF of patients with MPS II from the start of ICV idursulfase-β treatment up to week 100[2]



Hunterase ICV Injection 15 mg

Enzyme Replacement Therapy for MPS II (Hunter syndrome)

GC Biopharma

Clinical trial

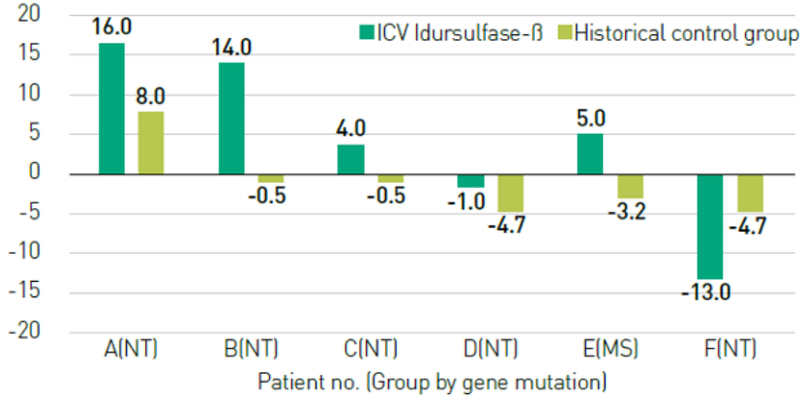
Secondary endpoints

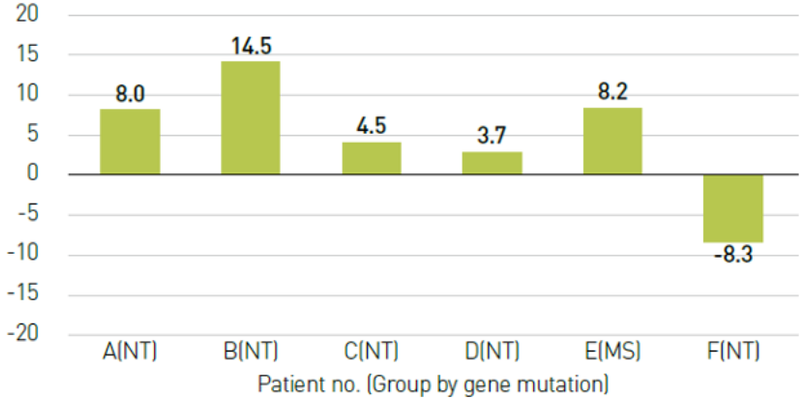
Developmental age (DA) determined by the Kyoto Scale of Psychological Development 2001 (KSPD) in the following three areas: postural-motor, cognitive-adaptive and language-social

Results

Monthly ICV administration of idursulfase-β maintained or increased DA in five of six patients compared with the historical control group receiving IV idursulfase. At 100 weeks (about 2 years) after starting this study, six patients who received ICV idursulfase-β had a 5.1-month increase in mean DA compared with 13 historical control patients who received only IV idursulfase.

Comparison with the historical control data in patients with MPS II[2)]





Group MS: characterized by missense mutations and presumed to have slight residual enzyme activity
Group NT: considered to have null type mutations, such as deletions, recombination with pseudogene, and nonsense mutations

Hunterase ICV Injection 15 mg

Enzyme Replacement Therapy for MPS II (Hunter syndrome)

GC Biopharma

Characteristics of Hunterase ICV inj.

API	Idursulfase beta
Composition (1 ml/vial)	15 mg/mL of idursulfase beta in 150 mM of sodium chloride and 0.05% of polysorbate 20
Indication	MPS II. Administration of Hunterase ICV Injection should be considered for patients with MPS II for which improvement of central nervous system symptoms is necessary.
Dosage and Administration	The usual dosage is 30 mg of idursulfase beta (genetic recombination) administered intracerebroventricularly (ICV) once every 4 weeks. Administer Hunterase ICV inj. without dilution over at least 1 min.

Serum-Free Production Process

Reduced risk of pathogen contamination (Mycoplasmas, Viruses, Prions, etc.)[1, 7]

Effective Viral Inactivation and Removal Steps

(Low pH Inactivation & Nanofiltration - Dual Clearance)
Improved safety against potential enveloped and non-enveloped virus contamination[8]

High Proportion of Active-Form Enzymes

High level of formylglycine-form peptides (79.40±0.92%)[9]

References

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Hunterase ICV Injection 15 mg

Enzyme Replacement Therapy for MPS II (Hunter syndrome)

GC Biopharma

For more information, Please Scan the QR codes below.

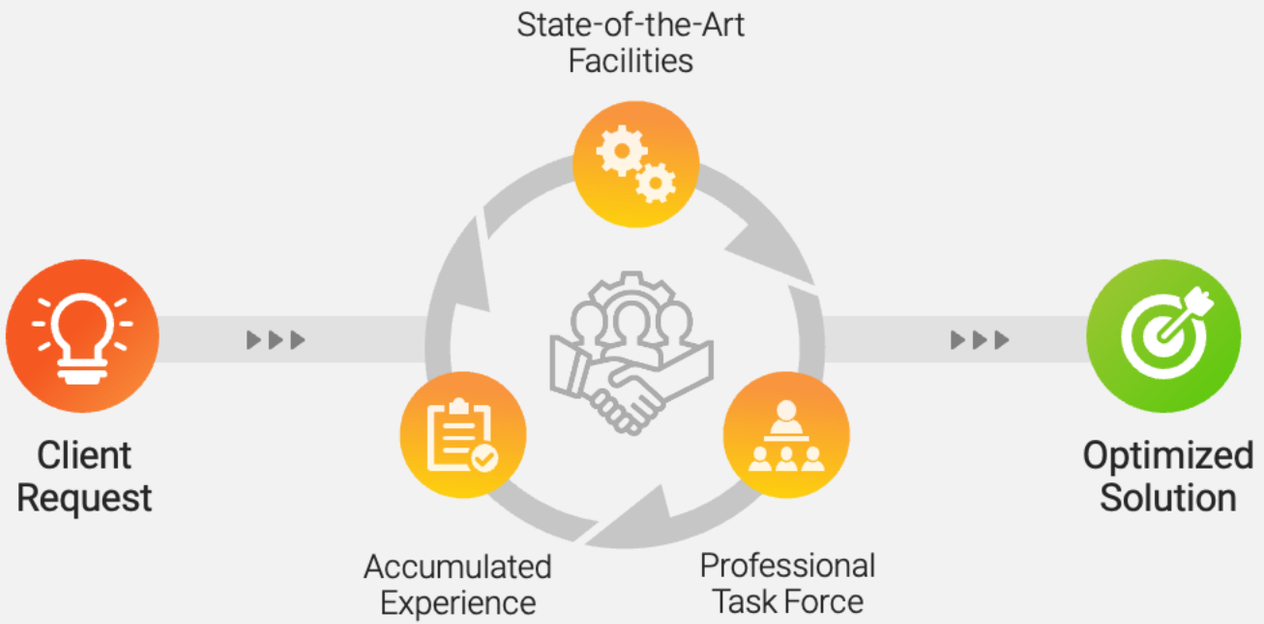
(Phase I/II) Impact of intracerebroventricular enzyme replacement therapy in patients with neuronopathic mucopolysaccharidosis type II, 2021

The efficacy of intracerebroventricular idursulfase-beta enzyme replacement therapy in mucopolysaccharidosis II murine model, 2018

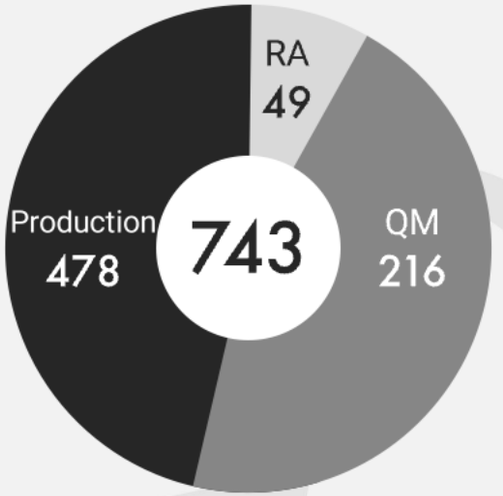
GC Biopharma

Our Customized Aseptic Fill & Finish Service

Brand New Manufacturing Sites



CMO Professional Personnel (DP+QM+RA)



Filling Solutions

From small to large scale production (5L - 1,000L)

Packaging Solutions

Diverse packaging format

Quality Management System

Regulatory track records (68 countries)

GC Biopharma

Our Customized Aseptic Fill & Finish Service

No.1 Aseptic Fill & Finish CMO Capacity in Korea

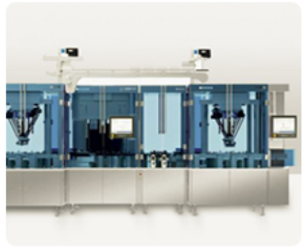
All our Quality System Satisfies cGMP		
Change Control System	Deviation System	Out of Specification System
Supplier Management System	Product Complaint System	Training System
Warehousing System	Recall System	IT System
Equipment Life Cycle Management System	Laboratory System	Document Management System

Site 1_Ochang

Brand New Manufacturing Sites

Established	2010 / 2019
Location	Ochang, South Korea
Area (F&F)	131,959 m^2
Products	Plasma & Recombinant Proteins, mRNA, AAV, C&GT
Key Services	Aseptic Fill & Finish, Logistics
Containers	Vials

- WHO PQ/ Ministry of Food and Drug Safety authorization completed/ FDA
- Formulation - filling - Lyo - packaging - release
- High speed Isolator line (Vial) & BSL-2
- Automatic visual inspection
- Automatic labeling and packaging system
- Automated warehouse-barcode system



Site 2_Hwasun (WHO PQ approved plant for global vaccine production)

Brand New Manufacturing Sites

Established	2010
Location	Hwasun, South Korea
Area (F&F)	98,963 m^2
Products	Vaccines
Key Services	Aseptic Fill & Finish
Containers	Vial & Pre-filled syringe

- WHO PQ/ Ministry of Food and Drug Safety authorization completed/ FDA
- Formulation - filling - Lyo - packaging - release
- Liquid Vials Filling (BSL 2 Available)
- Automatic visual inspection
- Automatic labeling and packaging system
- Packaging Aggregation system / serialization
- mRNA Facilities (Drug Substance) for 2025

GC Biopharma

Boldness and Passion in our History

This is the path GC Biopharma has taken

1967

Establishment

For half a century, GC has taken the difficult path of developing 'Medicinal drugs that are difficult to make, but essential' with the devotion to help build a society where everyone can enjoy a happy life without suffering from diseases.

1971

1st Plasma fractionation plant

Korea's 1st blood plasma fractionation plant

1983

World's 3rd vaccine against hepatitis B

Becomes third pharmaceutical company in the world to obtain product license for hepatitis-B vaccine **[Hepavax-B]**

1988

World's 1st vaccine against hemorrhagic fever with renal syndrome

Becomes first pharmaceutical company in the world to obtain product license for vaccine against hemorrhagic fever with renal syndrome **[Hantavax]**

GC Biopharma

Boldness and Passion in our History

This is the path GC Biopharma has taken

1993

World's 2nd vaccine against varicella

Becomes second company in the world to obtain product license for varicella vaccine **[Suduvax]**

2008

World's 4th Recombinant hemophilia A treatment

Fourth company in the world to obtain product license for recombinant hemophilia-A treatment **[GreenGene]**

2011

GC FLU TIV(SDV) Prequalified WHO

2012

World's 2nd ERT for MPS II

The world's 2nd ERT **[Hunterase] (Idursulfase beta)** has been developed and approved in Korea

GC Biopharma

Boldness and Passion in our History

This is the path GC Biopharma has taken

2021

World's 1st Antibiotic –free varicella vaccine

2021

World's 1st ERT for Neuronopathic MPSII

The world's 1st ERT for Nueornopathic MPS II [Hunterase ICV Inj.] has been developed and approved in Japan

2023

WHO Pre-Qualification for BARYCELA inj.

WHO Pre-Qualification for BARYCELA inj.

WHO Pre-Qualification for Hwasun plant

WHO Pre-Qualification for Filling and Finish plant of Ochang Plant

2023

IVIG 10% FDA Approval & Successful lunching

We always welcome the challenge of developing new medicine.

GC Biopharma